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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Watson et al.

Continuation Application of International Application No. PCT/US99/27805

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For: Method and Compositions for Diagnosis and Treatment of Cancer Based on the Transcription Factor ETS2

Attorney Docket No.: 10545-014-999

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Pursuant to 37 C.F.R. § 1.111, please consider the following amendments and remarks prior to examination of the above-identified application on the merits.

IN THE CLAIMS

Cancel claims 1-39 without prejudice.

Please add the following new claims:

--40. A method of killing a cancer cell that expresses the ets2 gene, comprising delivering to the cancer cell an effective amount of a chemotherapeutic agent or radiation, and an effective amount of an antisense nucleic acid molecule that is complementary to a region of the human ets2 cDNA as shown in Figure 6.

41. A method of treatment of a cancer in a subject, comprising the steps of:

(a) delivering to the cells of the cancer an effective amount of an antisense nucleic acid molecule that is complementary to a region of the human ets2 cDNA as shown in Figure 6; and

(b) administering to the subject with the cancer an effective amount of a chemotherapeutic agent or radiation.

42. The method of claim 40, wherein the cancer cell displays resistance to the chemotherapeutic agent.

43. The method of claim 41, wherein the cancer is refractory to treatment with the chemotherapeutic agent.

44. The method of claim 40, wherein said effective amount of the chemotherapeutic agent is less than the amount of the agent that is needed to kill the cancer cell when the agent is used alone.

45. The method of claim 41, wherein said effective amount of the chemotherapeutic agent is less than the amount of the agent that is used to treat the cancer when the agent is used alone.

46. The method of claim 40 wherein the antisense nucleic acid molecule is delivered to the cancer cell before the chemotherapeutic agent.

47. The method of claim 41 wherein the antisense nucleic acid molecule is delivered to the cells of the cancer concurrently with the administration of the chemotherapeutic agent.

48. The method of claim 40, wherein the cancer cell is a prostate cancer cell.

49. The method of claim 40, wherein the cancer cell is that of a cancer selected from the group consisting of liver cancer, cervical cancer, ovarian cancer, breast cancer, lung cancer, bladder cancer, kidney cancer, colon cancer, cancer of the rectum, and melanoma.

50. The method of claim 41, wherein the cancer is prostate cancer.

51. The method of claim 41, wherein the cancer is selected from the group consisting of liver cancer, cervical cancer, ovarian cancer, breast cancer, lung cancer, bladder cancer, kidney cancer, colon cancer, cancer of the rectum, and melanoma.

52. The method of claim 40 or 41, wherein said chemotherapeutic agent is one selected from the group consisting of alkylating agent, methylating agent, platinum-containing agent, antimetabolite or topoisomerase II inhibitor.

53. The method of claim 40 or 41, wherein said chemotherapeutic agent forms adducts in the DNA of the cancer cell.

54. The method of claim 40 or 41, wherein said chemotherapeutic agent is cisplatin.

55. The method of claim 40 or 41, wherein said chemotherapeutic agent is carboplatin.

56. The method of claim 40 or 41, wherein said antisense nucleic acid molecule is a RNA molecule produced by expressing an expression vector comprising a nucleotide sequence encoding the antisense RNA operably linked to a promoter.

57. The method of claim 56, wherein the expression vector is an adenovirus vector or an adeno-associated virus vector.

58. The method of claim 56, wherein the expression vector is delivered by direct injection of naked DNA of the expression vector.

59. The method of claim 56, wherein the expression vector is delivered by use of a delivery complex.

60. The method of claim 40 or 41, wherein said antisense nucleic acid molecule is an oligonucleotide that consists of at least 10 nucleotides.

61. The method of claim 40 or 41, wherein said antisense nucleic acid molecule is an oligonucleotide that consists of 10 to 50 nucleotides.

62. The method of claim 40 or 41, wherein said antisense nucleic acid molecule is complementary to a region of the human ets2 gene selected from the group consisting of the 5' non-translated region, the coding region, and the 3' non-translated region of the human ets2 gene.

63. The method of claim 40 or 41, wherein said antisense nucleic acid molecule comprises at least one modified phosphate backbone.

64. The method of claim 40 or 41, wherein the modified phosphate backbone comprises a phosphorothioate.

65. The method of claim 40 or 41, wherein said antisense nucleic acid molecule comprises at least one modified sugar moiety.

66. The method of claim 40 or 41, wherein said antisense nucleic acid molecule comprises at least one modified base moiety.

67. The method of claim 40 or 41, wherein the modified base moiety is 5-methylcytosine.--

REMARKS

Claims 1-39 have been canceled, and new claims 40-67 added, to more particularly point out and distinctly claim that which Applicants regard as the invention. The subject matter of the new claim recitations is fully supported in the specification. In

particular, support for new claims 40-67 is found in the specification as set forth in the chart below.

Claim Nos.	Support in Specification
40	page 70, lines 23-30, page 16, lines 19-22
41	page 70, lines 23-30, page 52, lines 20-24, page 53, lines 8-11, page 16, lines 19-22
42, 43	page 70, lines 1-4, page 72, lines 21-23
44, 45	page 72, lines 25-29
46, 47	page 72, lines 1-6
48, 49, 50, 51	page 20, lines 28-29, page 78, lines 6-9
52, 54, 55	page 71, lines 1-4
53	page 70, lines 28-30
56	page 62, lines 19-23
57	page 64, lines 8; 21-22
58, 59	page 62, line 29 to page 63, line 26
60, 61, 62	page 54, line 29 to page 55, line 8
63, 64	page 56, lines 20-21
65	page 56, lines 17-19
66, 67	page 56, lines 3-16

CONCLUSION

Applicants respectfully request that the amendments be entered and made of record in the instant application. An early allowance is earnestly requested.

Respectfully submitted,

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Enclosure